L Number	Hits	Search Text	DB	Time stamp
1	2296	cornell-$.as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:52
7	89	genvec.as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:52
13	0	(gen adj2 vec).as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:52
19	0	gen-vec.as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:52
25	2375	cornell-$.as. or genvec.as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:52
31	14	(cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
37	175	(serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:55
43	365	ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:55
49	2	((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and ((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35"))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:56
55	2	((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and (((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and ((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35")))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:56
61	2	(((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and ((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35"))) or (((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and (((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1)) and ((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35"))))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:57
67	377	(ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50) or ((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:57
73	2	(ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50) and ((cornell-$.as. or genvec.as.) and (chimer$3 adj2 fiber$1))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 18:57
79	5	(ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50) and (chimer$3 adj2 fiber$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:05
85	8	((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35")) and adenovir$4 and (chimer$3 adj2 fiber$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:05

91	5	(((serotype or adenovirus) adj2 ("11" or "14" or "16" or "21" or "34" or "35")) and adenovir$4 and (chimer$3 adj2 fiber$1)) not ((ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50) and (chimer$3 adj2 fiber$1))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
97	33	havenga-$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
103	129	vogels-$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
109	102	bout-$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
115	10	havenga-$.in. and vogels-$.in. and bout-$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
121	224	havenga-$.in. or vogels-$.in. or bout-$.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:29
127	1	(havenga-$.in. or vogels-$.in. or bout-$.in.) and ((hybrid or chimer$3) adj2 fiber$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:32
133	113	introgene-$.as.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:31
139	0	introgene-$.as. and ((hybrid or chimer$3) adj2 fiber$1)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/16 19:32

(FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002

```
L1          177 S (HAVENGA, ?)/IN,AU
L2         1774 S (VOGELS, ?)/IN,AU
L3          812 S (BOUT, ?)/IN,AU
L4         2674 S L1 OR L2 OR L3
L5          635 S AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50
L6         2276 S (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR
3
L7           13 S L5 AND L4
L8            6 DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)
L9           17 S L4 AND L6
L10          13 S L9 NOT L7
L11          13 DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)
L12           8 S L10 AND (FIBER (S) (CHIMER? OR HYBRID))
L13          30 S L5 AND (FIBER (S) (CHIMER? OR HYBRID))
L14          23 S L13 NOT L4
L15           8 DUPLICATE REMOVE L14 (15 DUPLICATES REMOVED)
L16          27 S L6 AND (FIBER (S) (CHIMER? OR HYBRID))
L17          16 S L16 NOT L14
L18          12 DUPLICATE REMOVE L17 (4 DUPLICATES REMOVED)
```

```
Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1636GXL

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08   "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09   BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09   ZDB will be removed from STN
 NEWS  5  Apr 19   US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
 NEWS  6  Apr 22   Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
 NEWS  7  Apr 22   BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22   Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03   New e-mail delivery for search results now available
 NEWS 10  Jun 10   MEDLINE Reload
 NEWS 11  Jun 10   PCTFULL has been reloaded
 NEWS 12  Jul 02   FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22   USAN to be reloaded July 28, 2002;
                   saved answer sets no longer valid
 NEWS 14  Jul 29   Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30   NETFIRST to be removed from STN
 NEWS 16  Aug 08   CANCERLIT reload
 NEWS 17  Aug 08   PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08   NTIS has been reloaded and enhanced
 NEWS 19  Aug 19   Aquatic Toxicity Information Retrieval (AQUIRE)
                   now available on STN
 NEWS 20  Aug 19   IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19   The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26   Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03   JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16   Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16   Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16   CA Section Thesaurus available in CAPLUS and CA

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.
```

```
  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *


FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002

=> file medline embase biosis caplus

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 19:39:23 ON 16 SEP 2002

FILE 'EMBASE' ENTERED AT 19:39:23 ON 16 SEP 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'BIOSIS' ENTERED AT 19:39:23 ON 16 SEP 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (havenga, ?)/in,au

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L1          177 (HAVENGA, ?)/IN,AU

=> s (vogels, ?)/in,au

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L2         1774 (VOGELS, ?)/IN,AU

=> s (bout, ?)/in,au

'IN' IS NOT A VALID FIELD CODE
'IN' IS NOT A VALID FIELD CODE
L3          812 (BOUT, ?)/IN,AU

=> s l1 or l2 or l3

L4         2674 L1 OR L2 OR L3

=> s ad11 or ad14 or ad16 or ad21 or ad34 or ad35 or ad50

L5          635 AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50

=> s (adenovir? or serotype) (2w) (11 or 14 or 16 or 21 or 34 or 35 or 50)

L6         2276 (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR 35
                OR 50)

=> s l5 and l4

L7           13 L5 AND L4

=> duplicate remove l7

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
```

PROCESSING COMPLETED FOR L7
L8 6 DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)

=> d ibib ab l8 1-6

L8 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391872 CAPLUS
DOCUMENT NUMBER: 136:396973
TITLE: Complementing cell lines expressing adenovirus serotype-specific E1B genes for the propagation of E1-deleted adenoviruses
INVENTOR(S): **Vogels, Ronald**; Havenga, Menzo Jans Emco; Mehtali, Majid
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040665	A2	20020523	WO 2001-NL824	20011114

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-713678 A 20001115
AB A packaging cell line capable of complementing recombinant adenoviruses based on serotypes from subgroup B, preferably adenovirus type 35. The cell line is preferably derived from primary, diploid human cells (e.g., primary human retinoblasts, primary human embryonic kidney cells and primary human amniocytes) which are transformed by adenovirus E1 sequences either operatively linked on one DNA mol. or located on two sep. DNA mols., the sequences being operatively linked to regulatory sequences enabling transcription and translation of encoded proteins. Also disclosed is a cell line derived from PER.C6 (ECACC deposit no. 96022940), which cell expresses functional **Ad35** E1B sequences. The **Ad35**-E1B sequences are driven by the E1B promoter or a heterologous promoter and terminated by a heterologous poly-adenylation signal (like HBV polyA). The new cell lines are useful for producing recombinant adenoviruses designed for gene therapy and vaccination. The cell lines can also be used for producing human recombinant therapeutic proteins such as human growth factors and human antibodies. In addn., the cell lines are useful for producing human viruses other than adenovirus such as influenza virus, herpes simplex virus, rotavirus, measles virus.

L8 ANSWER 2 OF 6 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001198465 MEDLINE
DOCUMENT NUMBER: 21136894 PubMed ID: 11238859
TITLE: Improved adenovirus vectors for infection of cardiovascular tissues.
COMMENT: Erratum in: J Virol 2001 Jun;75(11):5440
AUTHOR: **Havenga M J**; Lemckert A A; Grimbergen J M;

Vogels R; Huisman L G; Valerio D; **Bout A**; Quax P H

CORPORATE SOURCE: Crucell Holland B.V., 2301 CA Leiden, The Netherlands.. m.havenga@crucell.com

SOURCE: JOURNAL OF VIROLOGY, (2001 Apr) 75 (7) 3335-42. Journal code: 0113724. ISSN: 0022-538X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010723
Entered Medline: 20010405

AB To identify improved adenovirus vectors for cardiovascular gene therapy, a library of adenovirus vectors based on adenovirus serotype 5 (Ad5) but carrying fiber molecules of other human serotypes, was generated. This library was tested for efficiency of infection of human primary vascular endothelial cells (ECs) and smooth muscle cells (SMCs). Based on luciferase, LacZ, or green fluorescent protein (GFP) marker gene expression, several fiber chimeric vectors were identified that displayed improved infection of these cell types. One of the viruses that performed particularly well is an Ad5 carrying the fiber of **Ad16** (Ad5.Fib16), a subgroup B virus. This virus showed, on average, 8- and 64-fold-increased luciferase activities on umbilical vein ECs and SMCs, respectively, compared to the parent vector. GFP and lacZ markers showed that approximately 3-fold (ECs) and 10-fold (SMCs) more cells were transduced. Experiments performed with both cultured SMCs and organ cultures derived from different vascular origins (saphenous vein, iliac artery, left interior mammary artery, and aorta) and from different species demonstrated that Ad5.Fib16 consistently displays improved infection in primates (humans and rhesus monkeys). SMCs of the same vessels of rodents and pigs were less infectable with Ad5.Fib16 than with Ad5. This suggests that either the receptor for human **Ad16** is not conserved between different species or that differences in the expression levels of the putative receptor exist. In conclusion, our results show that an Ad5-based virus carrying the fiber of **Ad16** is a potent vector for the transduction of primate cardiovascular cells and tissues.

L8 ANSWER 3 OF 6 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2001163834 MEDLINE

DOCUMENT NUMBER: 21161183 PubMed ID: 11263771

TITLE: Infection efficiency of type 5 adenoviral vectors in synovial tissue can be enhanced with a type 16 fiber.

AUTHOR: Goossens P H; **Havenga M J**; Pieterman E; Lemckert A A; Breedveld F C; **Bout A**; Huizinga T W

CORPORATE SOURCE: Leiden University Medical Center, The Netherlands.

SOURCE: ARTHRITIS AND RHEUMATISM, (2001 Mar) 44 (3) 570-7. Journal code: 0370605. ISSN: 0004-3591.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200105

ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

AB OBJECTIVE: To obtain an adenoviral vector with increased infection efficiency in the synovial tissue compared with conventional vectors based on adenovirus serotype 5 (Ad5), without compromising the specificity of infection. METHODS: Coxsackie adenovirus receptor (CAR) expression was assessed in cultured synoviocytes. Chimeric adenoviruses based on Ad5 but carrying the DNA encoding the fiber of adenovirus from subgroup B (Ad11,

16, 35) or D (Ad24, 28, 33, 45, or 47) were constructed and produced on PER.C6 cells. The gene transfer efficiency of these chimera was tested on cultured synoviocytes and peripheral blood mononuclear cells (PBMC). RESULTS: No surface expression of CAR protein was observed on synoviocytes. CAR messenger RNA expression of synoviocytes was found to be low. Of all fiber chimeric vectors tested, vectors carrying the fiber of **Ad16** (Ad5.fib16) were most potent, yielding approximately150 times increased transgene expression in cultured synoviocytes compared with those of Ad5. Flow cytometry showed that the increase in transgene expression was caused by the transduction of higher percentages of synoviocytes and higher gene expression per synoviocyte. Experiments with 500 virus particles/cell of Ad5.GFP or Ad5.fib16.GFP resulted in an infection efficiency of 0.6% and 1% in PBMC and 43% and 76% in synoviocytes, respectively. CONCLUSION: Synoviocytes hardly express CAR, which hampers Ad5-mediated gene transfer. Ad5.fib16 is superior to Ad5 vectors for transducing synoviocytes, without compromising the specificity of infection. Our data suggest that Ad5.fib16-mediated gene transfer to synovial tissue improves the therapeutic window.

L8 ANSWER 4 OF 6 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001141799 MEDLINE
DOCUMENT NUMBER: 21079675 PubMed ID: 11212175
TITLE: The influence of synovial fluid on adenovirus-mediated gene transfer to the synovial tissue.
AUTHOR: Goossens P H; **Vogels R**; Pieterman E; **Havenga M J**; **Bout A**; Breedveld F C; Valerio D; Huizinga T W
CORPORATE SOURCE: Leiden University Medical Center, The Netherlands.
SOURCE: ARTHRITIS AND RHEUMATISM, (2001 Jan) 44 (1) 48-52. Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010308

AB OBJECTIVE: To determine the effect of synovial fluid (SF) from rheumatoid arthritis (RA) patients on adenovirus type 5 (Ad5)-mediated gene transfer to synoviocytes, and to explore new strategies for vector development based on the neutralization data obtained. METHODS: SF was derived from 63 randomly selected R4 patients. Ten samples were used to study the effect of SF on Ad5-mediated gene transfer in synoviocytes. IgG and <100-kd fractions were purified from these 10 SF, and their effect on gene transfer was determined. Neutralizing activity against wild-type Ad5 (wt-Ad5), wt-Ad26, wt-**Ad34**, wt-**Ad35**, and wt-Ad48 was tested in the SF from the remaining 53 patients. RESULTS: Seven of 10 SF samples inhibited Ad5-mediated gene transfer. Purified antibodies exhibited inhibition patterns similar to those seen with unfractionated SF. In 5 of 10 SF samples, low molecular weight fractions inhibited gene transfer at low dilutions. Neutralization of wt-**Ad35** by SF from RA patients was less frequent than neutralization of other wt-Ad tested (4% versus 42-72%; n = 53). CONCLUSION: SF from 70% of the RA patients contained neutralizing antibodies that hamper Ad5-mediated gene transfer to synoviocytes. The activity of neutralizing antibodies may be circumvented in the majority of RA patients when vectors based on an **Ad35** backbone are used.

L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:368622 CAPLUS
DOCUMENT NUMBER: 133:27392

TITLE: Chimeric adenoviral vectors specific for gene transfer
to smooth muscle cells, and/or endothelial cells
INVENTOR(S): **Havenga, Menzo Jans Emco**; Bout, Abraham; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031285	A1	20000602	WO 1999-NL717	19991122
W: AM, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MA, MD, MG, MN, MW, PL, RU, SD, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NO 9905697	A	20000522	NO 1999-5697	19991119
ZA 9907213	A	20000522	ZA 1999-7213	19991119
EP 1020529	A2	20000719	EP 1999-203878	19991119
EP 1020529	A3	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9959600	A1	20000525	AU 1999-59600	19991122
CA 2318492	AA	20000602	CA 1999-2318492	19991122
JP 2000157289	A2	20000613	JP 1999-332033	19991122

PRIORITY APPLN. INFO.: EP 1998-203921 A 19981120
WO 1999-NL717 W 19991122

AB The invention provides chimeric adenoviral vectors with tissue tropism of smooth muscle cells, and/or endothelial cells (but not of liver cells) used for gene transfer in gene therapy. The chimeric adenoviral vectors is constructed by switching the functional part (fiber protein subunit) of adenoviral capsid protein in adenovirus type 5 vector to that of a subgroup B adenovirus, preferably adenovirus 16 (**Ad16**). The biodistribution of these chimeric vector after i.v. tail vein injection of rats and and their display differences in the endothelial and smooth muscle cell transduction are detd. The infection efficiency of Ad5 vector to smooth muscle cells, and/or endothelial cells can be increased significantly by changing the fiber subunit (esp. shaft and knob parts) of capsid protein to that of **Ad16**. In this way, the host immune response to recombinant viruses derived from the chimeric adenovirus vectors are greatly reduced. The contribution of cellular receptors such as CAR (Coxsackievirus and adenovirus receptor) or integrin to viral infection is also studied. Methods of prepg. various chimeric adenovirus vectors and using them to treat diseases, preferably cardiovascular diseases are also provided.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:822744 CAPLUS
DOCUMENT NUMBER: 134:1341
TITLE: Adenovirus derived gene delivery vehicles with limited antigenicity derived from adenovirus type 35
INVENTOR(S): **Bout, Abraham**; Vogels, Ronald; Havenga,

Menzo Jans Emco
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: Eur. Pat. Appl., 135 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1054064	A1	20001122	EP 2000-201738	20000516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2000070071	A1	20001123	WO 2000-NL325	20000516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 1999-201545 A 19990517

AB Adenoviral vectors for delivery of nucleic acids to animal cells use elements of adenovirus 35 (**Ad35**) to limit the immune response of a recipient to the delivery vehicle. Important factors in the immune response to the virus include penton and hexon proteins and the E3 gene product and these may be combined with elements of other adenoviruses, e.g. to alter tissue tropism. **Ad35** is a rare virus and antibodies to it were not detected in serum samples from 100 healthy volunteers and was rare in serum from cardiovascular disease and rheumatoid arthritis patients. A series of chimeric vectors contg. components of **Ad35** and adenovirus 5 (Ad5) were not neutralized by human serum that could neutralize Ad5. A series of vectors for the rapid construction of **Ad35**-based vectors is described. The construction of chimeric adenovirus vectors with altered tropisms is discussed. The complete sequence of **Ad35** is presented. Adenovirus 11 was also rarely found to be neutralized by neutralizing antiserum.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002

```
L1          177 S (HAVENGA, ?)/IN,AU
L2         1774 S (VOGELS, ?)/IN,AU
L3          812 S (BOUT, ?)/IN,AU
L4         2674 S L1 OR L2 OR L3
L5          635 S AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50
L6         2276 S (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR
3
L7           13 S L5 AND L4
L8            6 DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)
```

=> s l4 and l6

```
L9          17 L4 AND L6
```

=> s l9 not l7

L10 13 L9 NOT L7

=> duplicate remove l10

PROCESSING COMPLETED FOR L10
L11 13 DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)

=> s l10 and (fiber (s) (chimer? or hybrid))

L12 8 L10 AND (FIBER (S) (CHIMER? OR HYBRID))

=> d ibib ab l12 1-8

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391896 CAPLUS
DOCUMENT NUMBER: 136:382853
TITLE: Adenoviral replicons useful as the therapeutic vectors
in cancer therapy
INVENTOR(S): **Havenga, Menzo Jans Emco**; Brus, Ronald Hendrik Peter
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040693	A1	20020523	WO 2001-NL834	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1207205	A1	20020522	EP 2000-204097	20001120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: EP 2000-204097 A 20001120
US 2000-249965P P 20001120

AB The invention provides a method for identifying an adenoviral replicon capable of eliminating a target cell, comprising contacting a representative cell with said adenoviral replicon and observing any detrimental effect. Once said replicon has been identified, it can be used to specifically eliminate certain cells involved in disease, for instance tumor cells. Preferably, said replicon contacts, enters and replicates predominantly in diseased cells, causing a detrimental effect in said cells, while in non-diseased cells no or a tolerable detrimental effect is induced. Preferably, said adenoviral replicon comprises a recombinant adenovirus with a fusion between DNA from Ad5 and subgroup B adenoviral DNA. Methods for producing and purifying a replicon according to the invention is also herewith provided. The invention test and compare the replication efficiency and the influence of the virus entry on the replication of different adenovirus in human various tumor cell lines.

The results indicate that Ad5 and some selected **chimeric fiber** viruses are able to enter all the tested tumor cell lines but the B-group serotypes replicate better compared to Ad5 in human tumor cell lines. The D-group serotypes replicate very poorly in the human tumor cell lines. The generation of the progeny viruses are detected in selected adenovirus infected cells. Methods for producing and purifying a replicon according to the invention is also herewith provided.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:391383 CAPLUS
DOCUMENT NUMBER: 136:382852
TITLE: Adenoviral replicons useful as the therapeutic vectors in cancer therapy
INVENTOR(S): **Havenga, Menzo Jans Emco**; Brus, Ronald Hendrik Peter
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1207205	A1	20020522	EP 2000-204097	20001120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002040693	A1	20020523	WO 2001-NL834	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2000-204097 A 20001120
US 2000-249965P P 20001120

AB The invention provides a method for identifying an adenoviral replicon capable of eliminating a target cell, comprising contacting a representative cell with said adenoviral replicon and observing any detrimental effect. Once said replicon has been identified, it can be used to specifically eliminate certain cells involved in disease, for instance tumor cells. Preferably, said replicon contacts, enters and replicates predominantly in diseased cells, causing a detrimental effect in said cells, while in non-diseased cells no or a tolerable detrimental effect is induced. Preferably, said adenoviral replicon comprises a recombinant adenovirus with a fusion between DNA from Ad5 and subgroup B adenoviral DNA. The invention test and compare the replication efficiency and the influence of the virus entry on the replication of different adenovirus in human various tumor cell lines. The results indicate that Ad5 and some selected **chimeric fiber** viruses are able to enter all the tested tumor cell lines but the B-group serotypes replicate better compared to Ad5 in human tumor cell lines. The D-group serotypes replicate very poorly in the human tumor cell lines. The generation of the progeny viruses are detected in selected adenovirus

infected cells. Methods for producing and purifying a replicon according to the invention is also herewith provided.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:276175 CAPLUS
DOCUMENT NUMBER: 136:289909
TITLE: Gene delivery vectors of adenoviruses with tropism for hemopoietic stem cell and uses for gene therapy
INVENTOR(S): **Havenga, Menzo Jans Emco**; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029073	A2	20020411	WO 2001-NL731	20011004
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1195440	A1	20020410	EP 2000-203471	20001006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 2000-203471 A 20001006
US 2000-238830P P 20001006

AB The invention provides methods of gene therapy by using adenovirus vectors having tropism for hemopoietic stem cells as a gene delivery vector. Specifically, the invention utilizes the adenovirus vector with tropism for hemopoietic stem cells, which is provided by at least part of an adeno-viral fiber protein derived from an adenovirus type 2 serotype or functional equiv. and/or homolog as a vehicle for delivering a therapeutical gene to stem cells, for the treatment of Hurlers disease, Hunters disease, Sanfilippos disease, Morquois disease, Gaucher disease, Farbers disease, Niemann-pick disease, Krabbe disease, Metachromatic leukodystrophy, I-Cell disease, Fucosidose deficiency, Thalassemia and Erythropoietic porphyria, AIDS, cancer or other autoimmune diseases. The invention further provides adenovirus serotype 5 based plasmid vectors, viral vectors with **chimeric fiber** proteins.

L12 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:256492 CAPLUS
DOCUMENT NUMBER: 136:289947
TITLE: Recombinant adenovirus 5-based vectors with **chimeric fiber** and/or capsid for gene delivery in skeletal muscle cells or myoblasts
INVENTOR(S): **Havenga, Menzo Jans Emco**; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002027006	A1	20020404	WO 2001-NL703	20010925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1191104	A1	20020327	EP 2000-203336	20000926

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: EP 2000-203336 A 20000926
US 2000-235665P P 20000926

AB The invention provides means and methods for transduction of a skeletal muscle cell and/or a myoblast. Although transduction of a skeletal muscle cell is possible with adenovirus 5, Ad5 efficiently infects non-desirable liver cells, lung epithelia and other respiratory tissues, and this may cause side-effects. The present invention discloses a gene delivery vehicle with a tropism for a skeletal muscle cell comprising a Ad5 recombinant **chimeric** adenovirus with **chimeric** **fiber** and/or capsid protein with a decreased affinity for liver and lung cells. In a preferred aspect of the invention, said gene delivery vehicle comprises at least a tropism detg. part of an adenoviral fiber protein of subgroup B and/or F. More preferably, said gene delivery vehicle comprises at least part of a fiber protein of an **adenovirus** of stereotype (**11**, 16, 35, 40 and/or 51) or a functional part, deriv. and/or analog thereof. Use of said gene delivery vehicle for the prepn. of a medicament for the treatment of a disease which affects skeletal muscle or myoblasts, or for the prepn. of a vaccine is claimed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123234 CAPLUS
DOCUMENT NUMBER: 136:178976
TITLE: Chimeric adenovirus gene delivery vectors with cell type specificity for primary human chondrocytes and uses in treatment of cartilage disease
INVENTOR(S): **Havenga, Menzo Jans Emco**; Vogels, Ronald; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012523	A2	20020214	WO 2001-NL595	20010809

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001094348	A5	20020218	AU 2001-94348	20010809
US 2002115218	A1	20020822	US 2001-928262	20010810

PRIORITY APPLN. INFO.: EP 2000-202835 A 20000810
US 2000-224911P P 20000811
WO 2001-NL595 W 20010809

AB The present invention relates to a gene delivery vehicle comprising a recombinant adenovirus having a tropism for a primary human chondrocyte. By efficiently transducing a nucleic acid of interest into a primary chondrocyte, said gene delivery vehicle is able to at least in part improve the counteraction of cartilage disease. In one embodiment said recombinant adenovirus comprises a deletion in the gene encoding for fiber protein, which is replaced by a nucleic acid sequence encoding at least part of a fiber protein of a B-type adenovirus. The generation of adenovirus serotype 5 genomic plasmid clones and adenovirus serotype 5 based viruses with **chimeric fiber** proteins are described. Then primary chondrocytes are tested for expression of integrins, MHC class I, and CAR protein. Finally, transduction of human primary chondrocytes with recombinant **fiber chimeric** adenoviruses is detd.

L12 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:824199 CAPLUS
DOCUMENT NUMBER: 136:320004
TITLE: Highly efficient targeted transduction of undifferentiated human hematopoietic cells by adenoviral vectors displaying fiber knobs of subgroup B
AUTHOR(S): Knaan-Shanzer, Shoshan; Van Der Velde, Ietje; **Havenga, Menzo J. E.**; Lemckert, Angelique A. C.; De Vries, Antoine A. F.; Valerio, Dinko
CORPORATE SOURCE: Gene Therapy Section, Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, 2333 AL, Neth.
SOURCE: Human Gene Therapy (2001), 12(16), 1989-2005
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human hematopoietic stem cells (HSCs) are poorly transduced by vectors based on adenovirus serotype 5 (Ad5). This is primarily due to the paucity of the coxsackievirus-Ad receptor on these cells. In an attempt to change the tropism of Ad5, we constructed a series of chimeric E1-deleted Ad5 vectors in which the shaft and knob of the capsid fibers were exchanged with those of other Ad serotypes. In all these vectors, the Ad E1 region was replaced by an expression cassette contg. the cytomegalovirus immediate-early promoter and the gene for enhanced green fluorescent protein (GFP). Expts. performed in vitro showed an efficient transduction of umbilical cord blood (UCB) monocytes, granulocytes, and their precursors as well as the undifferentiated CD34+CD33-CD38-CD71- cells by Ad5 vectors carrying Ad subgroup B-specific **fiber chimeras** (Ad5FBs). In the latter subpopulation, which comprises less than 1% of the CD34+ cells and is highly enriched with cells repopulating immunodeficient mice, more than 90% of the cells were GFP+. Transduction by Ad5FBs of the less primitive fraction within UCB CD34+ cells was significantly lower. Actually, the transduction frequency and GFP level declined gradually with increased expression of the CD33, CD38, and CD71 antigens. Flow cytometric anal. of transduced UCB CD34+ cells that were cultured for 5 days on an allogeneic human bone marrow stroma layer showed maintenance of the phenotypically defined HSCs at levels

similar to those of control cultures. The latter finding indicates that neither the transduction procedure nor the high levels of GFP were toxic for these cells.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:50835 CAPLUS
DOCUMENT NUMBER: 134:126789
TITLE: Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)
INVENTOR(S): **Havenga, Menzo**; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004334	A2	20010118	WO 2000-NL481	20000707
WO 2001004334	A3	20010705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1067188	A1	20010110	EP 1999-202234	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1196594	A2	20020417	EP 2000-946537	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-142557P P 19990707
EP 1999-202234 A 19990708
WO 2000-NL481 W 20000707

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with **chimeric** adenoviruses comprising capsids derived from adenovirus 5 of which at least part of the adenovirus 5 **fiber** protein is replaced by a **fiber** protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete adenovirus serotype 5 genome, were constructed. From a plasmid the DNA encoding the adenovirus serotype 5 fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus serotypes. At the former E1 location in the genome of adenovirus serotype

5, any gene of interest can be cloned. A single transfection procedure of the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of adenovirus serotype 5 in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.

L12 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:28651 CAPLUS
DOCUMENT NUMBER: 134:111233
TITLE: Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)
INVENTOR(S): **Havenga, Menzo**; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: Eur. Pat. Appl., 95 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1067188	A1	20010110	EP 1999-202234	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001004334	A2	20010118	WO 2000-NL481	20000707
WO 2001004334	A3	20010705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1196594	A2	20020417	EP 2000-946537	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:
US 1999-142557P P 19990707
EP 1999-202234 A 19990708
WO 2000-NL481 W 20000707

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with **chimeric** adenoviruses comprising capsids derived from adenovirus 5 of which at least part of the adenovirus 5 **fiber** protein is replaced by a **fiber** protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete adenovirus serotype 5 genome, were constructed. From a plasmid the DNA encoding the adenovirus serotype 5 fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus

serotypes. At the former E1 location in the genome of adenovirus serotype
5, any gene of interest can be cloned. A single transfection procedure of
the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of adenovirus serotype 5 in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002
L1 177 S (HAVENGA, ?)/IN,AU
L2 1774 S (VOGELS, ?)/IN,AU
L3 812 S (BOUT, ?)/IN,AU
L4 2674 S L1 OR L2 OR L3
L5 635 S AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50
L6 2276 S (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR 3
L7 13 S L5 AND L4
L8 6 DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)
L9 17 S L4 AND L6
L10 13 S L9 NOT L7
L11 13 DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)
L12 8 S L10 AND (FIBER (S) (CHIMER? OR HYBRID))

=> s l5 and (fiber (s) (chimer? or hybrid))

L13 30 L5 AND (FIBER (S) (CHIMER? OR HYBRID))

=> s l13 not l4

L14 23 L13 NOT L4

=> duplicate remove l14

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L14
L15 8 DUPLICATE REMOVE L14 (15 DUPLICATES REMOVED)

=> d ibib ab l15 1-8

L15 ANSWER 1 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002003907 MEDLINE
DOCUMENT NUMBER: 21624265 PubMed ID: 11752156
TITLE: Adenovirus serotype 30 fiber does not mediate transduction via the coxsackie-adenovirus receptor.
AUTHOR: Law Lane K; Davidson Beverly L
CORPORATE SOURCE: Program in Gene Therapy, Program in Genetics, Department of
Internal Medicine, Neurology, and Physiology and Biophysics, University of Iowa College of Medicine, Iowa City, Iowa 52242, USA.
CONTRACT NUMBER: DK54759 (NIDDK)

HD33531 (NICHD)
HL07638-15 (NHLBI)
SOURCE: JOURNAL OF VIROLOGY, (2002 Jan) 76 (2) 656-61.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF447393
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020125
Entered Medline: 20020111

AB Prior work by members of our laboratory and others demonstrated that adenovirus serotype 30 (Ad30), a group D adenovirus, exhibited novel transduction characteristics compared to those of serotype 5 (Ad5, belonging to group C). While some serotype D adenoviruses bind to the coxsackie-adenovirus receptor (CAR), the ability of Ad30 **fiber** to bind CAR is unknown. We amplified and purified Ad30 and cloned the Ad30 **fiber** by overlap PCR. Alignment of Ad30 **fiber** with Ad3, **Ad35**, Ad5, Ad9, and Ad17 revealed that Ad30, like Ad9 and Ad17, has a shortened **fiber** sequence relative to that of Ad5. The knob region of **fiber** was 45% identical to that of the Ad5 knob regions. We made a **chimeric** recombinant virus (Ad5GFPf30) in which the Ad5 **fiber** (amino acids [aa]47 to 582) was replaced with Ad30 **fiber** sequences (aa 46 to 372), and CAR-mediated viral entry was determined on CAR-expressing Chinese hamster ovary (CHO) cells. While CAR expression significantly increased Ad5GFP-mediated transduction in CHO cells (from 1 to 36%), it did not enhance Ad5GFPf30 gene transfer. Binding of radiolabeled Ad5GFPf30 or Ad30 wild-type virus was also not improved by the expression of CAR. These results suggest that Ad30 **fiber** is distinct from Ad5, Ad9, and Ad17 fibers in its inability to direct transduction via CAR.

L15 ANSWER 2 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002297640 MEDLINE
DOCUMENT NUMBER: 22035355 PubMed ID: 12039033
TITLE: Adenovirus vectors containing **chimeric** type 5 and type 35 **fiber** proteins exhibit altered and expanded tropism and increase the size limit of foreign genes.
AUTHOR: Mizuguchi Hiroyuki; Hayakawa Takao
CORPORATE SOURCE: Division of Biological Chemistry and Biologicals, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, 158-8501, Tokyo, Japan.. mizguch@nihs.go.jp
SOURCE: GENE, (2002 Feb 20) 285 (1-2) 69-77.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020602
Last Updated on STN: 20020625
Entered Medline: 20020624

AB Adenovirus (Ad) **fiber** proteins are responsible for the initial attachment of the virion to the cell membrane. Most Ad vectors currently in use are based on the Ad type 5 (Ad5), which belong to subgroup C, and use the coxsackievirus and adenovirus receptors (CAR) as the initial receptor. **Ad35**, which belongs to subgroup B, recognizes unknown receptor(s) other than CAR. In this study, the feasibility of the Ad vector containing Ad5/35 **chimeric fiber** protein was examined in a wide variety of cell types, such as CAR-positive or -negative human tumor cells, rodent cells, and blood cells (a total of 20

cell types), and in mice in vivo. Transduction data suggested that the Ad vectors containing the Ad5/35 **chimeric fiber** protein exhibited altered and expanded tropism when compared with the Ad5-based vector. The **chimeric** vector also allows the packaging of larger foreign DNAs than the conventional Ad5-based vector, which can package approximately 8.1-8.2 kb of foreign DNA. The **chimeric** vector containing approximately 8.8 kb of foreign DNA was generated without affecting the viral growth rate and titer. These results suggested that inclusion of the **Ad35 fiber** protein into the Ad5-based vector could lead to an improved efficiency in gene therapy and in gene transfer experiments, especially for the cells lacking in sufficient CAR expression.

L15 ANSWER 3 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001364405 MEDLINE
DOCUMENT NUMBER: 21318989 PubMed ID: 11426333
TITLE: Efficient infection of primitive hematopoietic stem cells by modified adenovirus.
AUTHOR: Yotnda P; Onishi H; Heslop H E; Shayakhmetov D; Lieber A; Brenner M; Davis A
CORPORATE SOURCE: Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX 77030, USA.
CONTRACT NUMBER: RO1 CA78792 (NCI)
SOURCE: GENE THERAPY, (2001 Jun) 8 (12) 930-7.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB Almost all studies of adenoviral vector-mediated gene transfer have made use of the adenovirus type 5 (Ad5). Unfortunately, Ad5 has been ineffective at infecting hematopoietic progenitor cells (HPC). **Chimeric** Ad5/F35 vectors that have been engineered to substitute the shorter-shafted **fiber** protein from **Ad35** can efficiently infect committed hematopoietic cells and we now show highly effective gene transfer to primitive progenitor subsets. An Ad5GFP and Ad5/F35GFP vector was added to CD34(+) and CD34(-)lineage(-) (lin(-)) HPC.
Only 5-20% of CD34(+) and CD34(-)lin(-) cells expressed GFP after Ad5 exposure. In contrast, with the Ad5/F35 vector, 30-70% of the CD34(+), 50-70% of the CD34(-)lin(-) and up to 60% of the CD38(-) HPC expressed GFP
and there was little evident cellular toxicity. Because of these improved results, we also analyzed the ability of Ad5/F35 virus to infect the hoechst negative 'side population' (SP) of marrow cells, which appear to be among the very earliest multipotent HPC. Between 51% and 80% of marrow SP cells expressed GFP. The infected populations retained their ability to
form colonies in two short-term culture systems, with no loss of viability. We also studied the transfer and expression of immunomodulatory
genes, CD40L (cell surface expression) and interleukin-2 (secreted). Both were expressed at immunomodulatory levels for >5 days. The ability of Ad5/F35 to deliver transgenes to primitive HPC with high efficiency and low toxicity in the absence of growth factors provides an improved means of studying the consequences of transient gene expression in these cells.

L15 ANSWER 4 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001031502 MEDLINE
DOCUMENT NUMBER: 20499049 PubMed ID: 11044071
TITLE: Dependence of adenovirus infectivity on length of the fiber

shaft domain.
AUTHOR: Shayakhmetov D M; Lieber A
CORPORATE SOURCE: Division of Medical Genetics, University of Washington, Seattle, Washington 98195, USA.
SOURCE: JOURNAL OF VIROLOGY, (2000 Nov) 74 (22) 10274-86. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001121

AB One of the objectives in adenovirus (Ad) vector development is to target gene delivery to specific cell types. Major attention has been given to modification of the Ad **fiber** knob, which is thought to determine virus tropism. However, among the human Ad serotypes with different tissue tropisms, not only the knob but also the length of the **fiber** shaft domain varies significantly. In this study we attempted to delineate the role of **fiber** length in coxsackievirus-adenovirus receptor (CAR)- and non-CAR-mediated infection. A series of Ad serotype 5 (Ad5) capsid-based vectors containing long or short fibers with knob domains derived from Ad5, Ad9, or **Ad35** was constructed and tested in adsorption, internalization, and transduction studies. For Ad5 or Ad9 knob-possessing vectors, a long-shafted **fiber** was critical for efficient adsorption/internalization and transduction of CAR/alphav integrin-expressing cells. Ad5 capids containing short CAR-recognizing fibers were affected in cell adsorption and infection. In contrast, for the **chimeric** vectors possessing **Ad35** knobs, which enter cells by a CAR/alphav integrin-independent pathway, **fiber** shaft length had no significant influence on binding or infectibility on tested cells. The weak attachment of short-shafted Ad5 or Ad9 knob-possessing vectors seems to be causally associated with a charge-dependent repulsion between Ad5 capsid and acidic cell surface proteins. The differences between short- and long-shafted vectors in attachment or infection were abrogated by preincubation of cells with polycations. This study demonstrates that the **fiber**-CAR interaction is not the sole determinant for tropism of Ad vectors containing **chimeric** fibers. CAR- and alphav integrin-mediated infections are influenced by other factors, including the length of the **fiber** shaft.

L15 ANSWER 5 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000148948 MEDLINE
DOCUMENT NUMBER: 20148948 PubMed ID: 10684271
TITLE: Efficient gene transfer into human CD34(+) cells by a retargeted adenovirus vector.
AUTHOR: Shayakhmetov D M; Papayannopoulou T; Stamatoyannopoulos G; Lieber A
CORPORATE SOURCE: Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, Washington 98195, USA.
CONTRACT NUMBER: P01 HL53750 (NHLBI)
R01 CA80192 (NCI)
R21 DK55590 (NIDDK)
SOURCE: JOURNAL OF VIROLOGY, (2000 Mar) 74 (6) 2567-83. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000413
Last Updated on STN: 20000413

Entered Medline: 20000403

AB Efficient infection with adenovirus (Ad) vectors based on serotype 5 (Ad5) requires the presence of coxsackievirus-adenovirus receptors (CAR) and alpha(v) integrins on cells. The paucity of these cellular receptors is thought to be a limiting factor for Ad gene transfer into hematopoietic stem cells. In a systematic approach, we screened different Ad serotypes for interaction with noncycling human CD34(+) cells and K562 cells on the level of virus attachment, internalization, and replication. From these studies, serotype 35 emerged as the variant with the highest tropism for CD34(+) cells. A **chimeric** vector (Ad5GFP/F35) was generated which contained the short-shafted **Ad35 fiber** incorporated into an Ad5 capsid. This substitution was sufficient to transplant all infection properties from **Ad35** to the **chimeric** vector. The retargeted, **chimeric** vector attached to a receptor different from CAR and entered cells by an alpha(v) integrin-independent pathway. In transduction studies, Ad5GFP/F35 expressed green fluorescent protein (GFP) in 54% of CD34(+) cells. In comparison, the standard Ad5GFP vector conferred GFP expression to only 25% of CD34(+) cells. Importantly, Ad5GFP transduction, but not Ad5GFP/F35, was restricted to a specific subset of CD34(+) cells expressing alpha(v) integrins. The actual transduction efficiency was even higher than 50% because Ad5GFP/F35 viral genomes were found in GFP-negative CD34(+) cell fractions, indicating that the cytomegalovirus promoter used for transgene expression was not active in all transduced cells. The **chimeric** vector allowed for gene transfer into a broader spectrum of CD34(+) cells, including subsets with potential stem cell capacity. Fifty-five percent of CD34(+) c-Kit(+) cells expressed GFP after infection with Ad5GFP/F35, whereas only 13% of CD34(+) c-Kit(+) cells were GFP positive after infection with Ad5GFP. These findings represent the basis for studies aimed toward stable gene transfer into hematopoietic stem cells.

L15 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:314000 BIOSIS
DOCUMENT NUMBER: PREV200100314000
TITLE: Gene transfer into human hematopoietic cells with chimeric adenovirus vectors, devoid of all viral genes.
AUTHOR(S): Shayakhmetov, Dmitry M. (1); Farrer, Denise; Papayannopoulou, Thalia; Stamatoyannopoulos, George (1); Lieber, Andre (1)
CORPORATE SOURCE: (1) Division of Medical Genetics, University of Washington, Seattle, WA USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 430a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Efficient infection with adenovirus (Ad) vectors based on serotype 5 requires the presence of Coxsackie-adenovirus receptors (CAR) and alphav integrins on cells. The paucity of these cellular receptors is thought to be a limiting factor for Ad gene transfer into hematopoietic stem cells. In a systematic approach, we screened different Ad serotypes for interaction with non-cycling human CD34+, MO7e and K562 cells on the level of virus attachment, internalization, and replication. From these studies, serotype 35 emerged as the variant with the highest tropism for CD34+ cells. A **chimeric** first generation adenovirus vector

(Ad5GFP/F35) was generated which contained the short-shafted **Ad35 fiber** incorporated into an Ad5 capsid. In transduction studies, Ad5GFP/F35 expressed GFP under control of the human cytomegalovirus (CMV) promoter in 54% of CD34+ cells. In comparison, the standard Ad5GFP vector conferred GFP expression to only 25%. The actual transduction efficiency was even higher than 54% because Ad5GFP/F35 viral genomes were found in GFP negative CD34+ cell fractions, indicating that the CMV promoter used for transgene expression was not active in all transduced cells. We found that transduction with Ad5GFP, but not Ad5GFP/F35, was restricted to a specific subset of CD34+ cells expressing alphav integrins. The **chimeric** vector allowed for gene transfer into a broader spectrum of CD34+ cells including subsets with potential stem cell capacity. 55% of CD34+/c-kit+ cells expressed GFP after infection with Ad5GFP/F35 whereas, only 13% of CD34+/c-kit+ cells were GFP positive after infection with Ad5GFP. On the basis of Ad5GFP/F35, a vector expressing GFP under the control of the mouse stem cell virus (MSCV) promoter was constructed. This vector also contained inverted repeats, able to mediate the formation of the vector genomes, devoid of all viral genes which are packaged into Ad particles (DELTAAd.IR). The deleted DELTAAd.IR vector also contained two AAV ITRs surrounding the MSCV-GFP expression cassette capable of mediating stable gene transfer into transduced cells. Detailed data on the transduction properties of the deleted **chimeric** adenovirus vectors as well as colony formation capacity of cell populations transduced with **chimeric** Ad5/35 adenovirus vectors will be presented and discussed.

L15 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:301979 BIOSIS
DOCUMENT NUMBER: PREV200100301979
TITLE: Sequential transduction of human hematopoietic stem cells with retargeted adenovirus vectors devoid of all viral genes encoding the ecotropic retrovirus receptor followed by an ecotropic retrovirus vector.
AUTHOR(S): Stecher, Hartmut (1); Shayakhmetov, Dmitry (1); Farrer, Denise (1); Stamatoyannopoulos, George (1); Lieber, Andre (1)
CORPORATE SOURCE: (1) Division of Medical Genetics, University of Washington, Seattle, WA USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 384b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The use of adenovirus vectors (Ad) and retrovirus vectors for gene therapy of human hematopoietic diseases has been hampered by low efficiency viral transduction of hematopoietic stem cells (HSC). This is in part due to absent or low level expression of the corresponding viral receptors on the cell surfaces. Those cells which are infected by Ad can express the transgene only transiently. Further problems occur from using first or second generation Ad, which can lead to severe cytotoxic and immunogenic reactions. In our current study, we attempted to circumvent these problems by using a retargeted Ad devoid of all viral genes. This Ad encodes the ecotropic retrovirus receptor (ecoR). Once the infected cells transiently express the ecoR these cells become accessible targets for transduction with an ecotropic retroviral vector. This ecotropic retroviral vector

encodes a therapeutic and/or marker gene and is able to express the transgene persistently. The Ad used for this sequential transduction strategy (i) shows much higher transduction efficiency in HSC due to its **chimeric fiber** structure, (ii) is supposed to lack cytotoxic and immunogenic side reactions because its genomic structure lacks all viral genes and (iii) expresses the transgene only transiently since deleted genomes are unstable in transduced cells. The Ad was made of a **chimeric**, heterologous **fiber** consisting of an adenovirus type 5 (Ad5) **fiber** tail and an **Ad11** **fiber** shaft and knob because previous studies demonstrated that **Ad11** was much better at transducing HSC than Ad5. The transduction of erythroleukemia K562 cells with this **chimeric** virus encoding enhanced green fluorescent protein (EGFP) showed an efficiency of 65% at a multiplicity of infection (MOI) of 5. This is in contrast to only 3% when Ad5-EGFP was used at the same MOI. Similar studies to test transduction efficiency in CD34+ cells are in progress. A bicistronic expression cassette encoding ecoR and EGFP, controlled by the murine stem cell virus LTR (MSCV), and flanked on both sides by two 1.2kb inverted homologous sequences was cloned into the E1-deleted region of Ad5/11. We demonstrated formation and packaging of the 7.9kb deleted genome (DELTAAd/ecoR-EGFP). Currently, we are performing sequential transduction studies in human CD34+ cells with DELTAAd/ecoR-EGFP in combination with an ecotropic retroviral vector to test the long term survival of the transduced cells in SCID-NOD mice.

L15 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:322007 BIOSIS
DOCUMENT NUMBER: PREV200100322007
TITLE: High efficiency gene transfer to normal and malignant hematopoietic precursor cells using a chimeric adenovirus.
AUTHOR(S): Yotnda, Patricia (1); Onishi, Haroaki (1); Heslop, Helen (1); Brenner, Malcolm (1); Shayakhmetov, Dmitri; Lieber, Andre; Davis, Alan (1)
CORPORATE SOURCE: (1) Baylor College of Medicine, Houston, TX USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 218a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DOCUMENT TYPE: Article; Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Almost all studies of Adenoviral vector gene transfer have made use of the Adenovirus type 5 serotype. Unfortunately, Ad5 has generally been ineffective at transducing hemopoietic progenitor cells (HPC). **Chimeric** Adenovirus Type 5 vectors that have been engineered to substitute the shorter-shafted **fiber** protein from Adenovirus type 35 can transduce cells apparently lacking CAR or alpha(v) integrins required for Ad5 binding. We find that these vectors have the ability to rapidly transduce even the most phenotypically primitive subset of HPC when they are used at low viral concentration even in the absence of growth factors. An Ad5GFP and Ad5/35GFP vector was added to CD34+ and to CD34- lineage- human marrow progenitor cells. Transduction used a 6 hr co-incubation of the cells with the virus (1000 vp) in the absence of growth factors. Twenty-four hours after infection, cells were analyzed by flow cytometry for eGFP expression. Only 5-20% of CD34+ and CD34-lineage-cells expressed eGFP after Ad5 exposure. In contrast, with the **Ad35** pseudotyped vector, 30-70% of the CD34+ and 50-70% CD34-lineage-cells were positive for eGFP expression. The eGFP expression was detectable as soon as 6hr post-infection, when 24hr was necessary to

reach discernible expression for Ad5 infected cells. Because of these improved results, we also analyzed the ability of the **chimeric** virus to infect the Hoechst negative "Side Profile" population of CD34- marrow cells, which appear to be amongst the very earliest hematopoietic progenitor cells (Goodell MA et al Nat Med. 1997 Dec;3(12):1337-45). Between 51% and 80% of SP bone marrow cells expressed eGFP 24-hr post-infection. The transduced CD34+ and CD34- lin- populations retained their ability to form colonics in short and long term culture systems, with no significant loss of viability. Moreover, a high level of expression was also obtained with the **chimeric** vector but not with Ad5 in unstimulated malignant blasts from patients with CD34+ and CD34- AML and in the CD5 positive B cells of patients with B-CLL. The ability of **chimeric** Ad5/35F to deliver transgenes to normal and malignant hematopoietic stem cells with high efficiency and low toxicity in the absence of growth factors provides an improved means of studying the consequences of transient gene expression in these cells.

```
=> d his

     (FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002
L1          177 S (HAVENGA, ?)/IN,AU
L2         1774 S (VOGELS, ?)/IN,AU
L3          812 S (BOUT, ?)/IN,AU
L4         2674 S L1 OR L2 OR L3
L5          635 S AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50
L6         2276 S (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR
3
L7           13 S L5 AND L4
L8            6 DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)
L9           17 S L4 AND L6
L10          13 S L9 NOT L7
L11          13 DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)
L12           8 S L10 AND (FIBER (S) (CHIMER? OR HYBRID))
L13          30 S L5 AND (FIBER (S) (CHIMER? OR HYBRID))
L14          23 S L13 NOT L4
L15           8 DUPLICATE REMOVE L14 (15 DUPLICATES REMOVED)

=> s l6 and (fiber (s) (chimer? or hybrid))

L16         27 L6 AND (FIBER (S) (CHIMER? OR HYBRID))

=> s l16 not l14

L17         16 L16 NOT L14

=> duplicate remove l17

DUPLICATE PREFERENCE IS 'MEDLINE, EMBASE, BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n

PROCESSING COMPLETED FOR L17
L18          12 DUPLICATE REMOVE L17 (4 DUPLICATES REMOVED)

=> d ti l18 1-12


L18  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2002 ACS
TI   Adenoviral replicons useful as the therapeutic vectors in cancer therapy

L18  ANSWER 2 OF 12  CAPLUS  COPYRIGHT 2002 ACS
TI   Gene delivery vectors of adenoviruses with tropism for hemopoietic stem
     cell and uses for gene therapy
```

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Recombinant adenovirus 5-based vectors with **chimeric fiber** and/or capsid for gene delivery in skeletal muscle cells or myoblasts

L18 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Chimeric adenovirus gene delivery vectors with cell type specificity for primary human chondrocytes and uses in treatment of cartilage disease

L18 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Adenoviral replicons useful as the therapeutic vectors in cancer therapy

L18 ANSWER 6 OF 12 MEDLINE DUPLICATE 1
TI Use of a Chimeric Adenovirus Vector Enhances BMP2 Production and Bone Formation.

L18 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)

L18 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)

L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Highly efficient targeted transduction of undifferentiated human hematopoietic cells by adenoviral vectors displaying fiber knobs of subgroup B

L18 ANSWER 10 OF 12 MEDLINE DUPLICATE 2
TI A capsid-modified adenovirus vector devoid of all viral genes: assessment of transduction and toxicity in human hematopoietic cells.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Adenoviral vectors for cell specific infection and integration of transforming DNA using **chimeric fiber** proteins to define cell-specificity

L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
TI Chimeric adenoviral vectors specific for gene transfer to smooth muscle cells, and/or endothelial cells

=> d ibib ab l18 1-12

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391896 CAPLUS
DOCUMENT NUMBER: 136:382853
TITLE: Adenoviral replicons useful as the therapeutic vectors
in cancer therapy
INVENTOR(S): Havenga, Menzo Jans Emco; Brus, Ronald Hendrik Peter
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040693	A1	20020523	WO 2001-NL834	20011119

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1207205 A1 20020522 EP 2000-204097 20001120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: EP 2000-204097 A 20001120
US 2000-249965P P 20001120

AB The invention provides a method for identifying an adenoviral replicon capable of eliminating a target cell, comprising contacting a representative cell with said adenoviral replicon and observing any detrimental effect. Once said replicon has been identified, it can be used to specifically eliminate certain cells involved in disease, for instance tumor cells. Preferably, said replicon contacts, enters and replicates predominantly in diseased cells, causing a detrimental effect in said cells, while in non-diseased cells no or a tolerable detrimental effect is induced. Preferably, said adenoviral replicon comprises a recombinant adenovirus with a fusion between DNA from Ad5 and subgroup B adenoviral DNA. Methods for producing and purifying a replicon according to the invention is also herewith provided. The invention test and compare the replication efficiency and the influence of the virus entry on the replication of different adenovirus in human various tumor cell lines. The results indicate that Ad5 and some selected **chimeric fiber** viruses are able to enter all the tested tumor cell lines but the B-group serotypes replicate better compared to Ad5 in human tumor cell lines. The D-group serotypes replicate very poorly in the human tumor cell lines. The generation of the progeny viruses are detected in selected adenovirus infected cells. Methods for producing and purifying a replicon according to the invention is also herewith provided.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:276175 CAPLUS
DOCUMENT NUMBER: 136:289909
TITLE: Gene delivery vectors of adenoviruses with tropism for hemopoietic stem cell and uses for gene therapy
INVENTOR(S): Havenga, Menzo Jans Emco; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029073	A2	20020411	WO 2001-NL731	20011004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1195440 A1 20020410 EP 2000-203471 20001006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: EP 2000-203471 A 20001006
US 2000-238830P P 20001006

AB The invention provides methods of gene therapy by using adenovirus vectors having tropism for hemopoietic stem cells as a gene delivery vector. Specifically, the invention utilizes the adenovirus vector with tropism for hemopoietic stem cells, which is provided by at least part of an adeno-viral fiber protein derived from an adenovirus type 2 serotype or functional equiv. and/or homolog as a vehicle for delivering a therapeutical gene to stem cells, for the treatment of Hurlers disease, Hunters disease, Sanfilippos disease, Morquois disease, Gaucher disease, Farbers disease, Niemann-pick disease, Krabbe disease, Metachromatic leukodystrophy, I-Cell disease, Fucosidose deficiency, Thalassemia and Erythropoietic porphyria, AIDS, cancer or other autoimmune diseases. The invention further provides adenovirus serotype 5 based plasmid vectors, viral vectors with **chimeric fiber** proteins.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:256492 CAPLUS
DOCUMENT NUMBER: 136:289947
TITLE: Recombinant adenovirus 5-based vectors with **chimeric fiber** and/or capsid for gene delivery in skeletal muscle cells or myoblasts
INVENTOR(S): Havenga, Menzo Jans Emco; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002027006	A1	20020404	WO 2001-NL703	20010925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1191104	A1	20020327	EP 2000-203336	20000926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 2000-203336 A 20000926
US 2000-235665P P 20000926

AB The invention provides means and methods for transduction of a skeletal muscle cell and/or a myoblast. Although transduction of a skeletal muscle cell is possible with adenovirus 5, Ad5 efficiently infects non-desirable liver cells, lung epithelia and other respiratory tissues, and this may cause side-effects. The present invention discloses a gene delivery vehicle with a tropism for a skeletal muscle cell comprising a Ad5 recombinant **chimeric** adenovirus with **chimeric fiber** and/or capsid protein with a decreased affinity for liver and lung cells. In a preferred aspect of the invention, said gene

delivery vehicle comprises at least a tropism detg. part of an adenoviral fiber protein of subgroup B and/or F. More preferably, said gene delivery vehicle comprises at least part of a fiber protein of an **adenovirus** of stereotype (**11**, 16, 35, 40 and/or 51) or a functional part, deriv. and/or analog thereof. Use of said gene delivery vehicle for the prepn. of a medicament for the treatment of a disease which affects skeletal muscle or myoblasts, or for the prepn. of a vaccine is claimed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123234 CAPLUS
DOCUMENT NUMBER: 136:178976
TITLE: Chimeric adenovirus gene delivery vectors with cell type specificity for primary human chondrocytes and uses in treatment of cartilage disease
INVENTOR(S): Havenga, Menzo Jans Emco; Vogels, Ronald; Bout, Abraham
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012523	A2	20020214	WO 2001-NL595	20010809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001094348	A5	20020218	AU 2001-94348	20010809
US 2002115218	A1	20020822	US 2001-928262	20010810

PRIORITY APPLN. INFO.:
EP 2000-202835 A 20000810
US 2000-224911P P 20000811
WO 2001-NL595 W 20010809

AB The present invention relates to a gene delivery vehicle comprising a recombinant adenovirus having a tropism for a primary human chondrocyte. By efficiently transducing a nucleic acid of interest into a primary chondrocyte, said gene delivery vehicle is able to at least in part improve the counteraction of cartilage disease. In one embodiment said recombinant adenovirus comprises a deletion in the gene encoding for fiber protein, which is replaced by a nucleic acid sequence encoding at least part of a fiber protein of a B-type adenovirus. The generation of adenovirus serotype 5 genomic plasmid clones and adenovirus serotype 5 based viruses with **chimeric fiber** proteins are described. Then primary chondrocytes are tested for expression of integrins, MHC class I, and CAR protein. Finally, transduction of human primary chondrocytes with recombinant **fiber chimeric** adenoviruses is detd.

L18 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391383 CAPLUS
DOCUMENT NUMBER: 136:382852

TITLE: Adenoviral replicons useful as the therapeutic vectors
in cancer therapy
INVENTOR(S): Havenga, Menzo Jans Emco; Brus, Ronald Hendrik Peter
PATENT ASSIGNEE(S): Crucell Holland B.V., Neth.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1207205	A1	20020522	EP 2000-204097	20001120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002040693	A1	20020523	WO 2001-NL834	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2000-204097 A 20001120
US 2000-249965P P 20001120

AB The invention provides a method for identifying an adenoviral replicon capable of eliminating a target cell, comprising contacting a representative cell with said adenoviral replicon and observing any detrimental effect. Once said replicon has been identified, it can be used to specifically eliminate certain cells involved in disease, for instance tumor cells. Preferably, said replicon contacts, enters and replicates predominantly in diseased cells, causing a detrimental effect in said cells, while in non-diseased cells no or a tolerable detrimental effect is induced. Preferably, said adenoviral replicon comprises a recombinant adenovirus with a fusion between DNA from Ad5 and subgroup B adenoviral DNA. The invention test and compare the replication efficiency and the influence of the virus entry on the replication of different adenovirus in human various tumor cell lines. The results indicate that Ad5 and some selected **chimeric fiber** viruses are able to enter all the tested tumor cell lines but the B-group serotypes replicate better compared to Ad5 in human tumor cell lines. The D-group serotypes replicate very poorly in the human tumor cell lines. The generation of the progeny viruses are detected in selected adenovirus infected cells. Methods for producing and purifying a replicon according to the invention is also herewith provided.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002408465 IN-PROCESS
DOCUMENT NUMBER: 22153324 PubMed ID: 12162816
TITLE: Use of a Chimeric Adenovirus Vector Enhances BMP2 Production and Bone Formation.
AUTHOR: Olmsted-Davis Elizabeth A; Gugala Zbigniew; Gannon Francis H; Yotnda Patricia; McAlhany Robert E; Lindsey Ronald W; Davis Alan R
CORPORATE SOURCE: Center for Cell and Gene Therapy, Departments of Pediatrics

and Orthopaedic Surgery, Baylor College of Medicine, Houston, TX 77030.
SOURCE: HUMAN GENE THERAPY, (2002 Jul 20) 13 (11) 1337-47. Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20020807
Last Updated on STN: 20020807

AB Recombinant adenoviral vectors have potential for the treatment of a variety of musculoskeletal defects and such gene therapy systems have been a recent research focus in orthopedic surgery. In studies reported here, two different adenovirus vectors have been compared for their ability to transduce human bone marrow mesenchymal stem cells (hBM-MSCs) and elicit bone formation in vivo. Vectors consisted either of standard adenovirus type 5 (Ad5) vector or a **chimeric** adenovirus type 5 vector that contains an **adenovirus** type **35 fiber** (Ad5F35), which has been recently demonstrated to bestow a different cellular tropism, and a complete cDNA encoding human bone morphogenetic 2 (BMP2). Studies were also conducted to compare the transduction efficiency of these vectors using enhanced green fluorescent protein (GFP). hBM-MSCs transduced with Ad5F35 vectors had higher levels of transgene expression than those transduced with Ad5 vectors. The results also demonstrate that hBM-MSCs lack the coxsackie-adenovirus receptor (CAR), which is responsible for cellular adsorption of Ad5. Therefore, the data suggest that Ad5 virus adsorption to hBM-MSCs is inefficient. Ad5BMP2- or Ad5F35BMP2-transduced hBM-MSCs were also compared in an in vivo heterotopic bone formation assay. Mineralized bone was radiologically identified only in muscle that received the Ad5F35BMP2 transduced hBM-MSCs. In summary, Ad5F35BMP2 can efficiently transduce hBM-MSCs leading to enhanced bone formation in vivo.

L18 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:50835 CAPLUS
DOCUMENT NUMBER: 134:126789
TITLE: Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)
INVENTOR(S): Havenga, Menzo; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004334	A2	20010118	WO 2000-NL481	20000707
WO 2001004334	A3	20010705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1067188	A1	20010110	EP 1999-202234	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
EP 1196594 A2 20020417 EP 2000-946537 20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-142557P P 19990707
EP 1999-202234 A 19990708
WO 2000-NL481 W 20000707

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with **chimeric** adenoviruses comprising capsids derived from adenovirus 5 of which at least part of the adenovirus 5 **fiber** protein is replaced by a **fiber** protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete adenovirus serotype 5 genome, were constructed. From a plasmid the DNA encoding the adenovirus serotype 5 fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus serotypes. At the former E1 location in the genome of adenovirus serotype 5, any gene of interest can be cloned. A single transfection procedure of the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of adenovirus serotype 5 in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.

L18 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:28651 CAPLUS
DOCUMENT NUMBER: 134:111233
TITLE: Infection with chimeric adenoviruses of cells negative for the adenovirus serotype 5 coxsackie adenovirus receptor (CAR)
INVENTOR(S): Havenga, Menzo; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: Eur. Pat. Appl., 95 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1067188	A1	20010110	EP 1999-202234	19990708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001004334	A2	20010118	WO 2000-NL481	20000707
WO 2001004334	A3	20010705		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1196594 A2 20020417 EP 2000-946537 20000707

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-142557P P 19990707
EP 1999-202234 A 19990708
WO 2000-NL481 W 20000707

AB The invention discloses a method for delivering a nucleic acid of interest to a host cell by means of a gene delivery vehicle based on adenoviral material. One of the problems assocd. with the development of effective gene therapy protocols for the treatment of disease is the limitation of the current vectors to effectively transduce cells in vivo. This problem is overcome with **chimeric** adenoviruses comprising capsids derived from adenovirus 5 of which at least part of the adenovirus 5 **fiber** protein is replaced by a **fiber** protein from a different adenovirus serotype. The gene delivery vehicle delivers a nucleic acid to the host cell by assocg. with a binding site and/or a receptor present on CAR-neg. cells, said binding site and/or receptor being a binding site and/or a receptor for adenovirus subgroups D and/or F. For this purpose, two or three plasmids, which together contain the complete adenovirus serotype 5 genome, were constructed. From a plasmid the DNA encoding the adenovirus serotype 5 fiber protein is essentially removed and replaced by linker DNA sequences which facilitate easy cloning. This plasmid subsequently serves as template for the insertion of DNA encoding the fiber protein derived from different adenovirus serotypes. At the former E1 location in the genome of adenovirus serotype 5, any gene of interest can be cloned. A single transfection procedure of the two or three plasmids together result in the formation of a recombinant chimeric adenovirus. The invention also describes the construction and use of plasmids consisting of distinct parts of adenovirus serotype 5 in which the gene encoding for fiber protein has been replaced with DNA derived from alternative human or animal serotypes.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:824199 CAPLUS

DOCUMENT NUMBER: 136:320004

TITLE: Highly efficient targeted transduction of undifferentiated human hematopoietic cells by adenoviral vectors displaying fiber knobs of subgroup B

AUTHOR(S): Knaan-Shanzer, Shoshan; Van Der Velde, Ietje; Havenga, Menzo J. E.; Lemckert, Angelique A. C.; De Vries, Antoine A. F.; Valerio, Dinko

CORPORATE SOURCE: Gene Therapy Section, Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, 2333 AL, Neth.

SOURCE: Human Gene Therapy (2001), 12(16), 1989-2005
CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human hematopoietic stem cells (HSCs) are poorly transduced by vectors based on adenovirus serotype 5 (Ad5). This is primarily due to the paucity of the coxsackievirus-Ad receptor on these cells. In an attempt to change the tropism of Ad5, we constructed a series of chimeric E1-deleted Ad5 vectors in which the shaft and knob of the capsid fibers

were exchanged with those of other Ad serotypes. In all these vectors, the Ad E1 region was replaced by an expression cassette contg. the cytomegalovirus immediate-early promoter and the gene for enhanced green fluorescent protein (GFP). Expts. performed in vitro showed an efficient transduction of umbilical cord blood (UCB) monocytes, granulocytes, and their precursors as well as the undifferentiated CD34+CD33-CD38-CD71- cells by Ad5 vectors carrying Ad subgroup B-specific **fiber chimeras** (Ad5FBs). In the latter subpopulation, which comprises less than 1% of the CD34+ cells and is highly enriched with cells repopulating immunodeficient mice, more than 90% of the cells were GFP+. Transduction by Ad5FBs of the less primitive fraction within UCB CD34+ cells was significantly lower. Actually, the transduction frequency and GFP level declined gradually with increased expression of the CD33, CD38, and CD71 antigens. Flow cytometric anal. of transduced UCB CD34+ cells that were cultured for 5 days on an allogeneic human bone marrow stroma layer showed maintenance of the phenotypically defined HSCs at levels similar to those of control cultures. The latter finding indicates that neither the transduction procedure nor the high levels of GFP were toxic for these cells.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 12 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2002026486 MEDLINE
DOCUMENT NUMBER: 21366065 PubMed ID: 11472104
TITLE: A capsid-modified adenovirus vector devoid of all viral genes: assessment of transduction and toxicity in human hematopoietic cells.
AUTHOR: Stecher H; Shayakhmetov D M; Stamatoyannopoulos G; Lieber A
CORPORATE SOURCE: Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, WA 98195, USA.
CONTRACT NUMBER: P01 HL53750 (NHLBI)
P30 DK 47754 (NIDDK)
R21 DK55590 (NIDDK)
SOURCE: MOLECULAR THERAPY, (2001 Jul) 4 (1) 36-44.
Journal code: 100890581. ISSN: 1525-0016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011205

AB Inefficient gene transfer has limited the success of gene therapy in the hematopoietic system. Here we develop a novel **chimeric** adenovirus (Ad) vector containing Ad **serotype 11** **fiber**-modified capsids and E1/E3 deleted viral genomes (Ad5/11) or genomes devoid of all viral genes (DeltaAd5/11). The capsid-modified vectors transduced human hematopoietic cells more efficiently than the unmodified Ad5-based vector. The absence of viral genes from the DeltaAd5/11 vector allowed for transduction without the associated toxicity seen with the first-generation E1/E3 deleted vector. **Chimeric** vectors were used for transient expression of the ecotropic retrovirus receptor (ecoR) in Mo7e cells (a CD34-positive, c-Kit-positive, growth-factor-dependent human cell line) as a model for human hematopoietic progenitor cells. Expression of ecoR conferred susceptibility to subsequent retroviral transduction. The DeltaAd5/11 vector used to express ecoR allowed for expansion of retrovirally transduced cells, whereas transduction with the first-generation Ad5/11 vector resulted in cytotoxicity and, over time, loss of cells expressing the retrovirus-vector-derived transgene.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:861825 CAPLUS
DOCUMENT NUMBER: 134:26078
TITLE: Adenoviral vectors for cell specific infection and integration of transforming DNA using **chimeric fiber** proteins to define cell-specificity
INVENTOR(S): Lieber, Andre; Shayakhmetov, Dmitry; Farrar, Denise; Papayannopoulou, Thalia
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073478	A2	20001207	WO 2000-US15442	20000601
WO 2000073478	A3	20010705		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1181382	A2	20020227	EP 2000-939570	20000601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-137213P P 19990601
US 1999-161097P P 19991022
WO 2000-US15442 W 20000601

AB The present invention provides for novel adenovirus vectors carrying a foreign sequence that can be stably and efficiently transferred into diverse cell types or tissues independently of the cell surface markers that are normally used for adenovirus binding and uptake. The vectors have minimal adenovirus sequences necessary for replication and DNA packaging and cell specificity is altered by modification of the fiber proteins to include ligands for novel cell types. Also provided are methods for producing such vectors and the use thereof for gene therapy to target a specific cell type or tissue.

L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:368622 CAPLUS
DOCUMENT NUMBER: 133:27392
TITLE: Chimeric adenoviral vectors specific for gene transfer to smooth muscle cells, and/or endothelial cells
INVENTOR(S): Havenga, Menzo Jans Emco; Bout, Abraham; Vogels, Ronald
PATENT ASSIGNEE(S): Introgene B.V., Neth.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031285	A1	20000602	WO 1999-NL717	19991122
W: AM, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, GD, GE, GH,				

GM, HR, HU, ID, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MA,
MD, MG, MN, MW, PL, RU, SD, SG, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

NO 9905697	A	20000522	NO 1999-5697	19991119	
ZA 9907213	A	20000522	ZA 1999-7213	19991119	
EP 1020529	A2	20000719	EP 1999-203878	19991119	
EP 1020529	A3	20000816			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

AU 9959600	A1	20000525	AU 1999-59600	19991122	
CA 2318492	AA	20000602	CA 1999-2318492	19991122	
JP 2000157289	A2	20000613	JP 1999-332033	19991122	

PRIORITY APPLN. INFO.: EP 1998-203921 A 19981120
WO 1999-NL717 W 19991122

AB The invention provides chimeric adenoviral vectors with tissue tropism of smooth muscle cells, and/or endothelial cells (but not of liver cells) used for gene transfer in gene therapy. The **chimeric** adenoviral vectors is constructed by switching the functional part (**fiber** protein subunit) of adenoviral capsid protein in adenovirus type 5 vector to that of a subgroup B **adenovirus**, preferably **adenovirus 16** (Ad16). The biodistribution of these chimeric vector after i.v. tail vein injection of rats and and their display differences in the endothelial and smooth muscle cell transduction are detd. The infection efficiency of Ad5 vector to smooth muscle cells, and/or endothelial cells can be increased significantly by changing the fiber subunit (esp. shaft and knob parts) of capsid protein to that of Ad16. In this way, the host immune response to recombinant viruses derived from the chimeric adenovirus vectors are greatly reduced. The contribution of cellular receptors such as CAR (Coxsackievirus and adenovirus receptor) or integrin to viral infection is also studied. Methods of prepg. various chimeric adenovirus vectors and using them to treat diseases, preferably cardiovascular diseases are also provided.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 19:39:08 ON 16 SEP 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 19:39:23 ON 16 SEP 2002

L1	177	S (HAVENGA, ?)/IN,AU
L2	1774	S (VOGELS, ?)/IN,AU
L3	812	S (BOUT, ?)/IN,AU
L4	2674	S L1 OR L2 OR L3
L5	635	S AD11 OR AD14 OR AD16 OR AD21 OR AD34 OR AD35 OR AD50
L6	2276	S (ADENOVIR? OR SEROTYPE) (2W) (11 OR 14 OR 16 OR 21 OR 34 OR 3
L7	13	S L5 AND L4
L8	6	DUPLICATE REMOVE L7 (7 DUPLICATES REMOVED)
L9	17	S L4 AND L6
L10	13	S L9 NOT L7
L11	13	DUPLICATE REMOVE L10 (0 DUPLICATES REMOVED)
L12	8	S L10 AND (FIBER (S) (CHIMER? OR HYBRID))
L13	30	S L5 AND (FIBER (S) (CHIMER? OR HYBRID))
L14	23	S L13 NOT L4
L15	8	DUPLICATE REMOVE L14 (15 DUPLICATES REMOVED)
L16	27	S L6 AND (FIBER (S) (CHIMER? OR HYBRID))
L17	16	S L16 NOT L14
L18	12	DUPLICATE REMOVE L17 (4 DUPLICATES REMOVED)